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ACTION OF DIGITALIS ON THE BLOOD-VESSELS.*

By T. LAUDER BRUNTON, M.D., D.Sc., in conjunction with ADOLPH BERNHARD MEYER, M.D.

INDEPENDENTLY of each other, and in different ways, we both arrived at the conclusion that digitalin causes contraction of the small blood-vessels.† Wishing to support our views by still more conclusive proofs, we took advantage of the opportunities afforded to us in the physiological laboratory of the Berlin University to perform together, in February, 1868, some experiments on the subject. We are perfectly aware of their incompleteness, but circumstances having prevented us from continuing them, and the departure of one of us for a distant land rendering it improbable that we shall be able to resume them together, we now publish their results.

We believed that by a comparison of the form of the curves indicating the blood-pressure before and after the injection of digitalin into the circulation, we should be able to determine exactly whether it caused contraction of the arterioles or not. The kymographion we employed was that of Ludwig, as modified by Traube, and the experiments were conducted on dogs in the following manner:—The animal being narcotised by hydrochlorate of morphia, a cannula was inserted into the crural artery, and a curve (fig. 1) showing the normal blood-pressure was described. Digitalin, suspended in a small quantity of distilled water, was then injected into the carotid artery, and pressure-curves again described. Injection into the artery was

* Reprinted from the *Journal of Anatomy and Physiology*, vol. vii. 1873

† T. Lauder Brunton *On Digitalis: with some Observations on the Urine*, London, 1868, p. 52, and A. Bernhard Meyer, *Zur Lehre von den Herzgiften in Untersuchungen aus dem physiologischen Laboratorium der Züricher Hochschule* herausgegeben von Professor Fick. Wien, 1869, p. 71.

employed because Blake* found that digitalin produced a much greater effect on the blood-pressure when introduced into the circulation in this way than if injected into a vein. A comparison of the tracings thus obtained, after the injection, with that of the normal pressure and pulse (fig. 1), showed a slow-

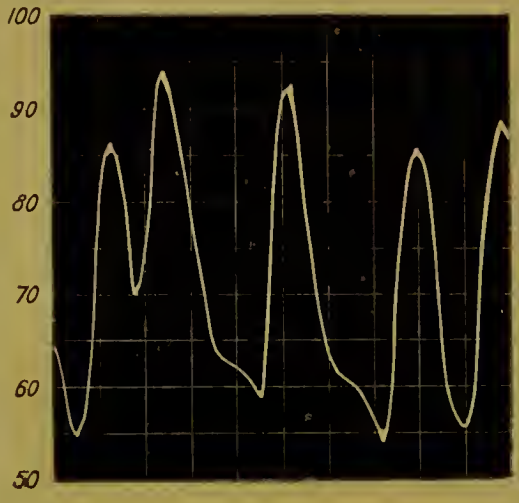

Fig. 1.

ing of the pulse, accompanied by an increase in the mean blood-pressure, while the height of the wave occasioned by each cardiac pulsation remained much the same (fig 2). The pres-

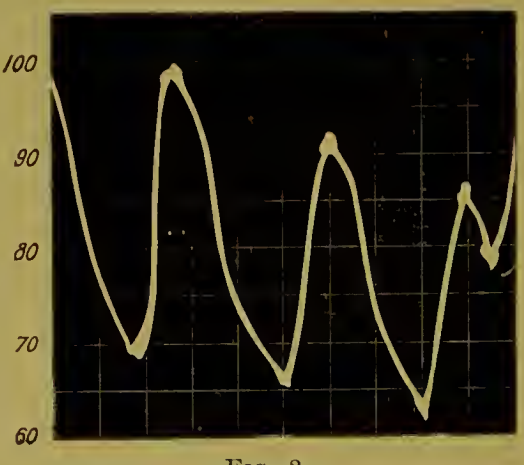

Fig. 2.

sure continued gradually to rise although the pulse not only became slower and slower, but the oscillations of the mercurial

* *Ed. Med. Journ.* 1839.

column at each pulsation diminished in extent (fig. 3). This rise could be due either to the heart propelling a greater quantity of blood into the aorta at each pulsation, or to the arteries contracting so as to hinder it from escaping from the arterial into the venous system. The diminished height of the pulse-wave seems sufficient of itself to negative the former idea, and to show that the increased pressure can only be due to contraction of the arterioles, but we think that a still clearer proof is afforded by the form of the wave. The time occupied in the ascent of the pressure-wave (indicated by the horizontal distance between the lowest and highest parts of the ascending limb) is nearly the same in figs. 1 and 3, but the descending limb of the latter sinks very gradually indeed, while in the

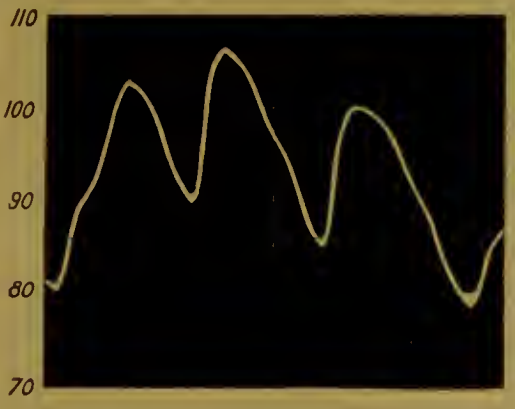

Fig. 3.

former it falls almost as quickly as it rises. What then is the explanation of this phenomenon? During the diastole of the heart, the sigmoid valves when healthy, as they were in this case, completely close the cardiac end of the aorta. The whole arterial system may then be compared to an elongated elastic vessel, from which fluid is issuing by a narrow opening. The greater the pressure of fluid in the vessel the more rapidly will it escape by the opening, the more quickly will the pressure consequently fall, and the more abrupt will be the descent of the pressure-curve. Now, the mean blood-pressure in the normal tracing is somewhat over 70 millimetres,* and the maxi-

* The true heights are of course nearly double these, but for convenient comparison with the tracings we have taken the numbers as they stand in the figures.

mum height of the wave 44, while in that taken when the action of the digitalin was greatest, the mean pressure is somewhat over 90 millimetres, and the maximum 104. The fall of pressure ought, therefore, to be more abrupt, but instead of this it is more gradual. This alteration cannot, we think, be explained by any oscillations of the mercurial column independently of the blood-pressure, and can only be due to contraction of the arterioles retarding the flow of blood from the arterial into the venous system during the cardiac diastole. In a recent paper,* Boehm considers that the rise in blood-pressure produced by digitalis, is chiefly due to the increased action of the heart, and that the condition of the arterioles has little or nothing to do with it. He seems, however, to interpret tracings of the blood-pressure in the arteries of mammals in the same way as those obtained from the excised heart of the frog, and apparently forgets that while in the latter the form of the diastolic as well as of the systolic curve depends on the heart alone, in the former the heart can have but little or no influence on the pressure in the arterial system during the diastole, since all communication between them is prevented by the closure of the sigmoid valves. The curves which he gives confirm our views, for they show the same gradual fall in the pulse-wave, after the injection of digitalis, that ours do, and being traced with Fick's spring-kymographion, are free from any fallacies due to oscillations of the mercurial column. The continued high pressure he observed during prolonged stoppage of the heart, and which he attributes to continuous cardiac systole, we would ascribe to contraction of the vessels so far as it is not due to changes in the respiration. If the arterioles were not contracted the pressure would fall, as, *e.g.*, in the experiments of Ludwig and Hafiz.†

We next attempted to ascertain whether the slowing of the pulse is due to a direct specific influence of the drug on the roots of the vagus as supposed by one of us,‡ or to the stimulation of these roots by the increased pressure of blood in the

* *Pflüger's Archiv*, vol. v, 190.
† Ludwig's *Arbeiten*, 1870.
‡ Brunton, *Op. cit.*

cranium produced by the contraction of the arterioles, as supposed by the other.* In order to do this we diminished the blood-pressure by the inhalation of nitrite of amyl after it had become high, and the pulse slow from the injection of digitalin. If the slowing of the pulse were due to a specific action of the digitalin on the vagus roots, it ought to continue although the pressure falls, but if due to stimulation of these roots by the high blood-pressure, it should disappear whenever the pressure is reduced. Our experiments showed that whenever the pressure fell after the inhalation of the nitrite of amyl the pulse became quick. It might thus appear that the slowing is due in part at least to the high pressure, and not altogether to a direct influence of the digitalin on the vagus; but this must be decided by farther experiment.

Lastly, we tried to discover whether digitalis causes contraction of the vessels by acting directly on their walls or on the vasomotor centre. This we sought to do by observing whether the injection of digitalin into the circulation caused any alteration in the calibre of the vessel of the rabbit's ear after the sympathetic nerve of the same side as well as both vagi had been divided in the neck. The vagi were divided in order to prevent the digitalin from slowing the heart, and thus disturbing the circulation, and the sympathetic to prevent any influence being transmitted to the vessels of the ear from the vasomotor centre. The results of these experiments were not constant, and we are unable to draw any definite conclusions from them; but the fact that the vessels of the ears were occasionally seen to empty themselves more quickly after the injection of digitalin than before, seems to us to indicate an action upon the walls of the vessels themselves.

The conclusions to which we have arrived are shortly, 1st, that digitalin causes contraction of the arterioles. This is proved by the small height of the pulse-wave, and by its descent becoming more gradual after the injection notwithstanding the increased blood-pressure. 2nd, that the slowing of the pulse is probably due in part to the increased blood-pressure which results from the contraction of the arterioles. We gladly take

* Meyer, *Op. cit.*

this opportunity of expressing our obligations to Professor Rosenthal for the assistance and advice which he so constantly and kindly afforded us, and to Herr Merck, of Darmstadt, to whose kindness we owe the digitalin we employed.

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